

AMENDMENT

Please amend the application without prejudice, without admission, without surrender of subject matter and without intention of creating any estoppel as to equivalents, as follows.

In the Claims

1. (Cancelled)
2. (Currently amended) ~~The modified VLD according to claim 1, wherein the A~~ modified monomeric non-antibody ligand V-like domain (VLD) comprising at least one CDR loop structure or part thereof that is modified or replaced such that
 - (i) the size of the CDR loop structure is ~~increased~~ altered when compared with the corresponding CDR loop structure in ~~[[the]]~~ an unmodified VLD; and/or
 - (ii) the modification or replacement results in formation of a disulphide bond within or between one or more of the CDR loop structures,wherein the non-antibody ligand is selected from the group consisting of CTLA-4, CD28 and ICOS.
3. (Cancelled)
4. (Currently amended) The modified VLD according to ~~claim 3~~ claim 2, wherein the size of the CDR loop structure is increased by at least two amino acid residues.
5. (Currently amended) The modified VLD according to ~~claim 3~~ claim 2, wherein the size of the CDR loop structure is increased by at least six amino acid residues.
6. (Currently amended) The modified VLD according to ~~claim 3~~ claim 2, wherein the size of the CDR loop structure is increased by at least nine amino acid residues.
7. (Currently amended) The modified VLD according to ~~claim 1 or claim 3~~ claim 2, wherein the binding affinity of the modified VLD is altered when compared with the unmodified VLD.
8. (Previously presented) The modified VLD according to claim 7, wherein the affinity of the modified VLD to at least one natural ligand of the unmodified VLD is reduced.
9. (Currently amended) The modified VLD according to ~~claim 1 or claim 3~~ claim 2, wherein the binding specificity of the modified VLD is different than that of the unmodified VLD.
10. (Cancelled)
11. (Cancelled)

12. (Currently amended) The modified VLD according to ~~claim 1~~ claim 2, wherein the non-antibody ligand is CTLA-4.

13. (Currently amended) The modified VLD according to ~~claim 1 or claim 3~~ claim 2, wherein one or more of the CDR loop structures is replaced with a binding determinant derived from a non-antibody polypeptide.

14. (Previously presented) The modified VLD according to claim 13, wherein the binding determinant is derived from somatostatin or haemagglutinin.

15. (Currently amended) The modified VLD according to ~~claim 1 or claim 3~~ claim 2, wherein one or more of the CDR loop structures is replaced with one or more CDR loop structures derived from an antibody or antibodies.

16. (Previously presented) The modified VLD according to claim 15, wherein the antibody or antibodies are derived from a rat, mouse, human, camel, llama or shark.

17. (Previously presented) The modified VLD according to claim 15, wherein the antibody or antibodies are selected from the camel antibody cAB-Lys3 and the human anti-melanoma antibody V86.

18. (Currently amended) The modified VLD according to ~~claim 1 or claim 3~~ claim 2, linked to a diagnostic reagent.

19. (Previously presented) The modified VLD according to claim 18, wherein the diagnostic reagent is selected from the group consisting of streptavidin, biotin, a radioisotope, a dye marker and an imaging reagent.

20. (Currently amended) A multivalent reagent comprising two or more modified VLDs as claimed in ~~claim 1~~ claim 2.

21. (Currently amended) The modified VLD or multivalent reagent according to ~~any one of claims 1, 3~~ claim 2 or 20, immobilised on a solid support or coupled to a biosensor surface.

22-27. (Cancelled)

28. (Currently amended) A ~~pharmaceutical~~ composition in a pharmaceutically acceptable carrier or diluent comprising a modified VLD or multivalent reagent as claimed in ~~any one of claims 1, 3~~ claim 2 or 20.

29-33. (Cancelled)

34. (Currently amended) The modified VLD according to ~~claim 1 or claim 3~~ claim 2, wherein at least two CDR loop structures or parts thereof are modified or replaced.

35. (Currently amended) The modified VLD according to ~~claim 1 or claim 3~~ claim 2, wherein three CDR loop structures or parts thereof are modified or replaced.

36. (Cancelled)

37. (Cancelled)

38. (Currently amended) ~~At least one~~ The modified monomeric ~~non-antibody ligand V-like domain (VLD) comprising at least one CDR loop structure or part thereof that is modified or replaced, such that~~ according to claim 2, wherein the solubility of the modified VLD is improved[[,]] when compared with [[an]] the unmodified VLD, ~~wherein the monomeric VLD is a binding moiety, and wherein the non-antibody ligand is CTLA-4, CD28 or ICOS.~~

39. (Cancelled)

40. (Cancelled)

41. (Currently amended) The modified VLD according to ~~claim 3~~ claim 2, wherein the size of the CDR loop structure is increased by one amino acid residue.